July 14, 2000

VIA HAND DELIVERY

Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services
Room 1-23
12420 Parklawn Drive
Rockville, MD 20857

00P-1406

74178 '00 JUL 14 P2:39

Re: **PETITION FOR STAY OF AGENCY ACTION**

Dear Madam or Sir:

This petition is submitted on behalf of the Compressed Gas Association and the National Welding Supply Association. The Compressed Gas Association ("CGA"), (1725 Jefferson Davis Highway, Suite 1004, Arlington, VA 22202), is a trade association whose more than 200 members are large and small manufacturers, distributors, suppliers, and transporters of gases, cryogenic liquids, and related products, including industrial, medical, and specialty gases in compressed or liquefied form. The CGA is a standards-setting organization whose mission is to develop and promote safety standards and safe practices for industrial and medical gases. The CGA maintains about 150 technical publications relating to this safety mission, of which approximately one–third are specifically cited in the Code of Federal Regulations (C.F.R.), making them legally mandated requirements (see C.F.R., Title 29, Occupational Safety and Health, and Title 49, Transportation).

CGA is joined in this petition by the National Welding Supply Association ("NWSA"), (1900 Arch Street, Philadelphia, PA, 19104). NWSA is a national trade association representing the interests of over 700 distributors of compressed gases and over 400 manufacturers of gases and related products. Many of these member companies supply compressed medical gases to hospitals, doctors' and dentists' offices, and clinics. NWSA's Safety Committee develops company safety and regulatory compliance programs for its members.

In this Petition, the CGA and NWSA request that, pursuant to 21 C.F.R. § 10.35, the Commissioner of Food and Drugs stay (1) presenting, conducting, publishing, or otherwise promulgating "Fresh Air" speeches/documents that delineate current Good Manufacturing Practice ("cGMP") requirements for compressed medical gases, and (2) the continued dissemination of previous Fresh Air speeches in any form, including videotapes or transcripts.[1] As demonstrated below, pursuant to Section 701(h) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 371(h), the Agency's proposed regulations

[1] See FDA, Fresh Air 1995 (Dec. 1995); FDA, Fresh Air 1996 (Dec. 4, 1996); FDA, Fresh Air 1997 (April 22, 1997); FDA, Fresh Air 1998 (May 13, 1998); FDA, Fresh Air 1998 (Nov. 10,

at 21 C.F.R. § 10.115,[2] the Agency's final regulations at 21 C.F.R. §§ 10.90(b)(9), 10.40(b), and Sections 4 and 10(e) of the Administrative Procedure Act, 5 U.S.C. §§ 553, 706, the Stay requested in this Petition should be granted.

I. Decision Involved

The decisions as to which CGA/NWSA seek a stay are FDA's future presentation, publishing, and promulgation of Fresh Air speeches/documents, and FDA continuing to make available previous Fresh Air speeches and materials--in videotapes, transcripts or any other form.

II. Action Requested

CGA/NWSA request that FDA promptly stay presenting, conducting, publishing, or otherwise promulgating Fresh Air speeches/documents, and continuing to make available previous Fresh Air speeches in any form.

III. Statement of Grounds

A. Regulatory History

Compressed gases, when intended for certain medical uses, have historically been regulated as prescription drugs. As such, FDA has required that they be manufactured, processed, packed, and held using "current good manufacturing practices," or "cGMPs." Specific cGMP requirements have been adopted by FDA for finished pharmaceuticals using notice and comment rulemaking. See 21 C.F.R. Parts 210 and 211. However, because of the uniqueness of the manufacturing and processing of compressed gases compared with finished pharmaceuticals which are in other, different dosage forms, FDA has, since at least 1978, taken the position that it needs to propose separate good manufacturing practice regulations applicable specifically to the medical gases industry. 43 Fed. Reg. 45014, 45027 (Sept. 29, 1978).

The final rule for cGMP regulations for human drug products was issued on September 29, 1978.[3] This rule left undefined the specific cGMP requirements for medical gases. The preamble to the final rule stated:

> The agency will propose specific cGMP regulations for compressed medical gases. Until such regulations can be proposed for public comment, comments received and evaluated, and a final regulation published, however, the

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1998); FDA, Fresh Air 1999 (Nov. 9, 1999); FDA, Fresh Air 2000 (Mar. 8, 2000). See Attachment 1 for the most recent version of Fresh Air.

[2] Administrative Practices and Procedures; Good Guidance Practices, 65 Fed. Reg. 7321 (Feb. 14, 2000).

[3] See 43 Fed. Reg. 45014 (Sept. 29, 1978).

> Commissioner concludes that the requirements in the more general cGMP regulations, with certain stated exceptions, are applicable.[4]

The FDA has, to date, never proposed cGMP regulations for medical gases, but the Agency continues to acknowledge the significant differences between medical gas and traditional pharmaceutical manufacturing activities.[5]

FDA issued medical gas cGMP guidelines in 1981, 1983, and 1989.[6] The 1989 Guideline is FDA's last formal statement of cGMP requirements for medical gases, and as a formal guideline, represents the logical benchmark for assessing current requirements in this area.[7] This guideline does not, however, accurately reflect FDA's current practice in the regulation of medical gas cGMP requirements, and the Agency has recognized and stated that the 1989 Guideline does not comport with its current standards.[8] For example, the 1989 Guideline includes no discussion of some of the more difficult issues of compliance for the medical gas industry (e.g., validation, air separation plant compliance obligations, issues involving quality assurance ("QA") review, etc.). Because the 1989 Guideline is skeletal and incomplete, it has created a regulatory vacuum, which has permitted the Fresh Air program to take on a significance that far exceeds its appropriate and lawful regulatory role, as described more below.

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4 Id. at 45027 (emphasis added).

5 See 43 Fed. Reg. 45014, 45027 (Sept. 29, 1978) and note 8.

6 See FDA, Compressed Medical Gas Guideline (June 1981); FDA, Compressed Medical Gas Guideline (Dec. 1983); FDA, Compressed Medical Gas Guideline (Revised) (Feb. 1989).

7 The introduction to the 1989 Guideline states: "A person may rely upon [this guideline] with assurance of its acceptability to FDA . . . This guideline describes practices and procedures for compressed medical gas (CMG) fillers (including companies engaged in home respiratory services) that constitute acceptable means of complying with certain sections of the current good manufacturing practice (CGMP) regulations for drug products (21 CFR Parts 210 and 211)." FDA, Compressed Medical Gas Guideline (Revised) (Feb. 1989) (emphasis added). This guideline has not been amended or revoked to date, and FDA continues to acknowledge that this document is the only formal Agency statement of cGMP requirements for medical gases. See Fresh Air 2000, at 2.

8 During the Fresh Air 2000 videoconference, FDA compliance official Duane Sylvia stated that the 1989 Guideline is "obsolete." Videotape: Fresh Air 2000 (FDA 2000). Also, each Fresh Air document issued from 1997 to the present has stated that the FDA is working to develop a new guidance document concerning medical gas cGMP requirements. See, e.g., FDA, Fresh Air 2000, at 2 ("There are no specific medical gas regulations ... We are currently working with industry to develop Fresh Air into the next official guidance document."). See Attachment 2 for a comparison between the 1989 Guideline and Fresh Air 2000 requirements.

B. The Role of Fresh Air

Since 1995, FDA has, in effect, set forth new medical gas cGMP requirements through Fresh Air speeches and related workshops and documents issued at least annually. The Fresh Air speeches and documents have significantly expanded, changed, and/or refined the 1989 Guideline requirements.[9] And, the rate of Fresh Air speeches and documents seems to be increasing. In 1995, 1996, and 1997, there was one Fresh Air speech/document. However, in 1998, two Fresh Air speeches were presented. Although only one Fresh Air program was presented in 1999, barely three months after the Fresh Air 1999 document was posted on the FDA's website, another Fresh Air program was given on March 15, 2000.[10]

All Fresh Air documents issued from 1997 to the present suggest they will form the basis for new guidelines,[11] but no Fresh Air documents have been published in the Federal Register for notice and comment, and there has been – and is – no formal, record-based mechanism for industry comment or interaction on these documents.

The detrimental impact on the medical gas industry of being regulated by so called "standards" set forth in a series of speeches that include extemporaneous as well as scripted materials cannot be underestimated. Indeed, FDA inspectors historically have undertaken compliance reviews of CGA/NWSA members based largely on standards recited in Fresh Air, and verbally cite to Fresh Air during inspections. Many of the standards cited from Fresh Air are highly specific requirements that are not contained in the 1989 Guideline (or the general cGMP regulations), as conveyed by Attachment 2, which compares the 1989 Guideline and Fresh Air 2000.

On March 3, 2000 representatives of the CGA met with staff from the House Commerce Committee, Subcommittee on Oversight and Investigations, to discuss many of these issues. Apparently as a result of that meeting, on April 27, 2000, Joseph C. Famulare, the Director of the Division of Manufacturing and Product Quality, Office of Compliance, Center for Drug Evaluation and Research, issued a memorandum to the Director, Office of Regional Operations, Office of Regulatory Affairs (Attachment 4), which noted that Fresh Air should not be cited as "regulatory requirements" in establishment inspection reports ("EIRs"), Forms 483, or Warning Letters issued by the Agency. CGA/NWSA appreciate this necessary step taken by the Agency, but for the reasons set forth in this petition, even if appropriate authorities within FDA abide by the terms of Mr. Famulare's memorandum, CGA/NWSA believe that the on-going initiation and promulgation of new Fresh Air programs, and the

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[9] See Attachment 3 for a list of some of the more significant changes made to the Fresh Air requirements in 1998 and 1999.

[10] The Fresh Air 2000 document was posted on FDA's website on March 8, 2000, and was presented live as a satellite broadcast entitled "Fresh Air 2000 Medical Gas Workshop" on March 15, 2000. Id.

[11] See note 1.

continued availability of previous Fresh Air transcripts and documents, must be stayed until the remaining problems described in this petition are addressed by the Agency. In short, the Famulare memorandum, while a very welcome development, merely addresses one small facet of the regulatory shortcomings of Fresh Air.

C. Legal Argument

The FDA's current regulation of medical gases cGMPs, including Fresh Air, is legally deficient in at least two ways. First, Fresh Air violates the requirements of the Administrative Procedure Act ("APA") that Agency regulations must be promulgated using notice and comment rulemaking, to give both the regulated industry and the public an opportunity to comment on newly proposed regulations or modifications to existing regulations, and to create a meaningful record for judicial review. Second, the current regulation of medical gases also violates significant provisions of the Food and Drug Administration Modernization Act of 1997 ("FDAMA") which established "good guidance practices" for FDA.

1. FDA's Presentation of Fresh Air Speeches and Issuance of Fresh Air Documents Violate the Administrative Procedure Act ("APA") Because They Are Arbitrary, Capricious, an Abuse of Discretion, or Otherwise Not in Accordance With Law.

The APA requires that federal agencies publish a notice of proposed rulemaking in the Federal Register, and give interested persons an opportunity to submit comments concerning proposed rules.[12] Further, the APA requires that the actions of federal agencies not be arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law.[13] FDA's Fresh Air speeches/documents violate the APA because they constitute substantive rules that have been promulgated without observance of notice and comment procedures, and because FDA's actions in promulgating and previously imposing these standards do not represent reasoned decisionmaking.

Fresh Air speeches/document are not merely policy statements or interpretative rules, but, rather, are substantive rules under the APA. The APA defines a "rule" as "an agency statement of general or particular applicability and future effect designed to implement, interpret, or prescribe law or policy."[14] The D.C. Circuit has stated that "[t]he primary distinction between a substantive rule -- really any rule -- and a general statement of policy . . . turns on whether an

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[12] 5 U.S.C. § 553; 5 U.S.C. § 706(2)(D). FDA has implemented these notice and comment requirements at 21 C.F.R. §10.90.

[13] 5 U.S.C. § 706(2)(A). Notice and comment rulemaking and informal adjudications of agencies are generally reviewed by courts under this standard.

[14] 5 U.S.C. § 551(4).

agency intends to bind itself to a particular legal position."[15] FDA has clearly treated its Fresh Air speeches/documents as binding on its own staff and on the regulated industry, and these speeches/documents specifically implement and prescribe FDA's cGMPs for the medical gas industry.[16] As noted throughout this petition, Agency staff have directly cited Fresh Air standards during inspections, Form 483 observances have closely mirrored or quoted Fresh Air standards, and FDA memoranda have directed FDA officials to Fresh Air Speech speeches/documents for further information on medical gas cGMP requirements. (It is precisely because of this reality that Mr. Famulare attempted to address these concerns in his April 27, 2000 memorandum (Attachment 4).)

FDA's Fresh Air speeches/documents represent de facto regulations because they have clearly been intended to be binding on the Agency's own staff and on the regulated industry.[17] Further, these regulations are substantive in that they have implemented and prescribed FDA's cGMP requirements for the medical gas industry. Agency staff have directly cited Fresh Air pronouncements during inspections, and many Form 483 observances have closely mirrored or directly quoted Fresh Air pronouncements. In addition, the authoritative nature of the Fresh Air speeches/documents is further evidenced by the language used therein describing the applicable requirements, e.g., "Each firm is required to establish . . .," "procedures . . . must be in writing . . .," etc.[18] Also, the Agency's March 1997 and June 1998 Human Drug cGMP Notes, a periodic memo to FDA personnel on cGMP issues on human use pharmaceuticals,[19] direct FDA personnel to Fresh Air documents for further information on medical gas "cGMP

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15 Syncor Internat'l Corp. v. Shalala, 127 F.3d 90, 94 (D.C. Cir. 1997).

16 Courts have determined that they should look to the practical reality of an agency's actions in determining whether such actions are rules, and will not exclusively rely on the agency's characterizations of such actions in making such determinations. See id. at 92 (FDA called its action "Guidance" and "Public Workshop;" after district court ruling, FDA conceded it was a rule).

17 FDA's definition of a "regulation" (i.e., "an agency rule of general or particular applicability and future effect issued under law administered by the Commissioner or relating to administrative practices or procedures") is nearly identical to the APA definition of a "rule" (i.e., "an agency statement of general or particular applicability and future effect designed to implement, interpret, or prescribe law or policy"). See 5 U.S.C. § 551(4), 21 C.F.R. § 10.3(a). Therefore, the indicia of a rule under the APA (e.g., meant to be binding on agency staff), properly should be considered indicia of a regulation under FDA's regulations. See Section III.C.2 of this Petition.

18 Such mandatory language appears throughout all of the Fresh Air presentations. For a full list of the presentations, see note 1.

19 FDA, Current Good Manufacturing Practice Issues on Human Use Pharmaceuticals, (Feb. 28, 2000) <http://www.fda.gov/cder/dmpc/cgmpnotes.htm> FDA's website information concerning Human Drug cGMP Notes states this publication represents level 2 guidance that presents the Agency's current thinking on cGMP issues.

requirements."[20] Based on the foregoing, FDA's Fresh Air speeches/documents have plainly exhibited the significant characteristics of regulations. The Agency must therefore properly develop these regulations pursuant to the requirements of the APA and its rulemaking regulations, and cease presenting and publishing future Fresh Air speeches/documents and continuing to provide previously published Fresh Air documents.

In recognizing the importance of an adequate administrative record to ensure appropriate judicial review, the courts have held that an agency, including FDA, has an obligation to consider all the evidence and provide adequate explanation for its decision in the administrative record.[21] Where an agency's regulation involves complicated scientific and technical issues, it is essential that the public have the opportunity to comment regarding government interpretation, to ensure that the record includes adequate consideration of the relevant evidence and to ensure a proper basis for judicial review in the event of challenge.

In determining whether an agency's actions are, under the APA, arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law, the courts have held that the principal inquiry is whether an agency's action constitutes "reasoned decisionmaking."[22] Lack of reasoned decisionmaking is evidenced by: (1) no record support for factual findings; (2) decisions contrary to facts in the record; (3) failure to disclose reasons for decisions; and (4) misunderstanding of the law.[23] As amply demonstrated above, FDA's continued promulgation of Fresh Air standards without a proper administrative record, without proper notice and comment, and without any kind of explanation or statement of the agency's basis for

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[20] See FDA, Gas what? Policy Questions on Medical Gases, (Feb. 28, 2000) <http://www.fda.gov/cder/compliance/gaswhat.htm>; FDA, Human Drug cGMP Notes (Volume 6, No. 2, June 1998); (Feb. 28, 2000) http://www.fda.gov/cder/hdn/cnotes68.htm>

[21] See City of Charlottesville v. Federal Energy Regulatory Commission, 661 F.2d 945, 950 (D.C. Cir. 1981); Asarco Inc. v. Environmental Protection Agency, 615 F.2d 1153, 1159 (9th Cir. 1980) (holding that an agency has a duty to consider all the evidence and to explain its decision fully). These principles have been applied to inadequate FDA decision-making in the past, where courts have reversed agency action that did not address significant substance and procedural concerns. See United States v. Nova Scotia Food Products Corp., 568 F.2d 240, 251 (2d. Cir. 1977) (stating that the "inadequacy of comment leads to arbitrary decision-making").

[22] See American Lung Ass'n v. EPA, 134 F.3d 388, 392 (D.C. Cir. 1998) ("we have always required the Administrator to 'cogently explain why [she] has exercised [her] discretion in a given manner'") (quoting Motor Vehicle Mfrs. Ass'n v. State Farm Mut. Auto. Ins. Co., 463 U.S. 29, 48 (1983)); cf. General Elec. Co. v. U.S. Dep't of Commerce, 128 F.3d 767, 774 (D.C. Cir. 1997) (by failing to explain changes from a proposed rule, the agency "failed to exercise reasoned decisionmaking"); Milk Indus. Found. v. Glickman, 967 F. Supp. 564, 570 (D.D.C. 1997) (reasoned decisionmaking precludes "a '[s]udden and unexplained change'") (quoting Smiley v. Citibank, 517 U.S. 735, 742 (1996)).

[23] See note 22.

establishing the standards, is far from reasoned decisionmaking. Rather it is, by definition, arbitrary, capricious, and an abuse of discretion.

2. FDA's Presentation of Fresh Air Speeches and Issuance of Fresh Air Documents Violates the Federal Food, Drug, and Cosmetic Act ("FDCA") and FDA's Regulations

Section 405 of the FDA Modernization Act of 1997 ("FDAMA") requires that FDA: (1) "develop guidance documents with public participation"; and (2) "ensure public participation prior to implementation" of guidance documents "that set forth initial interpretations of a statute or regulation, [and] changes in interpretation or policy that are of more than a minor nature. . . ."[24] The legislative history of FDAMA states that it is Congress' intention that FDA "will waive [the] requirement for prior public participation only in rare and extraordinary circumstances where there is a compelling interest."[25]

On February 14, 2000, FDA issued a proposed rule on Good Guidance Practices ("GGP's") setting forth procedures for the development, issuance, and use of guidance documents to advance the requirements of Section 405 of FDAMA.[26] The proposed rule elaborates on the role of GGP's in communicating FDA regulatory requirements and the Agency's commitment to implementing GGP's.[27] The proposed rule states, "[b]ecause the Agency's issuance of GGP's is an attempt to make its processes for initially communicating new or different regulatory expectations to a broad public audience consistent across the Agency . . . FDA should not use other methods or documents to informally provide this information."[28] Likewise, the proposed rule continues that the FDA agrees that it "should not develop or modify policies and procedures through informal mechanisms such as speeches or statements at meetings that it has not previously dealt with through regulation or prior guidances."[29]

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[24] Food and Drug Administration Modernization Act of 1997, Pub. L. No., 105-115, 111 Stat 2296 (1997) (emphasis added).

[25] See H.R. Rep. No. 105-310, 105th Cong., 1st Sess., at 74 (1997) (emphasis added).

[26] Administrative Practices and Procedures; Good Guidance Practices, 65 Fed. Reg. 7321 (2000). Note that Section 405 of FDAMA requires the GGP rule to have been finalized by July 1, 2000.

[27] The proposed rule states guidance documents: (1) "are those prepared for FDA staff, applicants/sponsors, and the public that describe the agency's interpretation of or policy on a regulatory issue;" (2) include documents related to the design, manufacturing, and testing of regulated products, and inspection and enforcement policies; and (3) do not include speeches. 65 Fed. Reg. 7321, 7323.

[28] Id. (emphasis added).

[29] Id. at 7327 (emphasis added).

"GGP's must be followed whenever interpretations of law or policy are not readily apparent from the statute, or regulations are first communicated to a broad public audience."[30]

In addition, the proposed rule reaffirms FDA's commitment to implementing GGP's. It states that, "on a regular basis, FDA Centers and Offices will monitor the development, issuance, and use of guidance documents to ensure that employees are following good guidance practices."[31] Moreover, the preamble to the proposed rule could not be more clear about the need for consistency in guidance or about the fact that such consistency is often undermined when agency employees informally communicate agency policy:

> The fundamental premise behind GGP's is increased consistency in the development, issuance, and use of guidance documents. The Agency is committed to ensuring that these principles are upheld, and urges the public to notify FDA of FDA employees first communicating agency policy through informal mechanisms such as speeches or statements at meetings.[32]

In direct conflict with FDAMA's explicit mandate and FDA's own proposed rule for GGP's, FDA employees have communicated new and different Agency policies for medical gases through informal mechanisms such as speeches and statements at meetings. Specifically, FDA employees have communicated new cGMP requirements for medical gases in informal Fresh Air speeches/documents and workshops.

FDA's promulgation, issuance, and enforcement of Fresh Air standards, without any public participation, plainly violate Section 405 of FDAMA and FDA's proposed rule for GGP's. As demonstrated by a comparison between the 1989 Guideline and recent Fresh Air documents, Fresh Air speeches/documents include new and expanded cGMP requirements that did not previously exist.[33] As discussed above in Section III.A. of this Petition, the 1989 Guideline

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[30] Id. at 7323-4 (emphasis added).

[31] Id. at 7325.

[32] Id. at 7327 (emphasis added).

[33] See Attachment 2 for a comparison between the 1989 Guideline and Fresh Air 2000 requirements. Fresh Air 2000 and previous versions of Fresh Air speeches/documents provide detailed additional requirements on at least the following nineteen discrete cGMP regulatory sections not addressed in any fashion in the 1989 Guideline: (1) 21 C.F.R. § 22(a) -- Quality Control Unit; (2) 21 C.F.R. § 25(a) -- Personnel Qualifications; (3) 21 C.F.R. § 34 -- Consultants; (4) 21 C.F.R. § 211.42 -- Design and Construction; (5) 21 C.F.R. § 211.67(a) -- Equipment Cleaning and Maintenance; (6) 21 C.F.R. § 211.68 -- Equipment Calibration; (7) 21 C.F.R. §§ 211.100(a), (b) -- Written Procedures; (8) 21 C.F.R. § 211.101(a) -- Charge-in of Components; (9) 21 C.F.R. § 211.103 -- Calculation of Yield; (10) 21 C.F.R. §§ 211.142, 150 -- Holding and Distribution; (11) 21 C.F.R. § 165(e) -- Testing and Release, Alternative Testing Methods; (12) 21 C.F.R. § 166 -- Stability Testing; (13) 21 C.F.R. §§ 211.180(a), 182 -- General Requirements and Equipment Cleaning and Use Log; (14) 21

includes no discussion of some of the more difficult and uncertain requirements of cGMP compliance for medical gases (e.g., validation, air separation plant compliance obligations, issues involving QA review, etc.), which are discussed in detail in FDA's Fresh Air speeches/documents.[34] Moreover, the Agency has not stopped at simply enunciating these new cGMP standards, but has immediately enforced those standards. A review of recent Warning Letters and Form 483s issued to medical gas manufacturers for noncompliance with cGMP requirements presents compelling evidence that FDA has implemented Fresh Air standards without any public participation -- many Warning Letters and Form 483s have cited noncompliance with specific requirements that are set forth in Fresh Air speeches/documents but are not discussed in the 1989 Guideline.[35]

Section 405 of FDAMA and FDA's proposed rule for GGP's require the FDA not to use methods or documents other than through properly developed guidance documents to communicate new or different regulatory expectations when interpretations of law are not readily apparent from the statute or regulations. The rapid and expansive changes to Fresh Air speeches/documents themselves year-to-year (and now month-to-month) evidence the ambiguous nature of how cGMP requirements apply to medical gases.[36] Therefore, pursuant to Section 405 of FDAMA and FDA's proposed rule for GGP's, FDA, at a minimum, should formally define the cGMP requirements for medical gases through a properly developed guidance document, and publish this guidance document in the Federal Register for notice and comment, instead of promulgating such requirements through informal Fresh Air speeches/documents.

C.F.R. § 211.186 -- Master Production and Control Records; (15) 21 C.F.R. § 211.192 -- Production Record Review; (16) 21 C.F.R. § 211.196 -- Distribution Records; (17) 21 C.F.R. § 211.198 -- Complain Files; (18) 21 C.F.R. § 211.204 -- Returned Drug Products; and (19) 21 C.F.R. § 211.208 -- Drug Product Salvaging.

[34] Id.

[35] As recognized by FDA, Warning Letters issued to medical gas manufacturers and distributors have stated that Fresh Air speeches contain information on how to comply with the cGMP requirements, and have provided Fresh Air documents as attachments to the Warning Letters. See, e.g., Warning Letter from Raymond V. Mlecko, District Director, Chicago District, FDA, to Emmanuel J. Likou, Chairman, Total Respiratory Services and Medical Equipment, Inc. (Aug. 11, 1999); Warning Letter from Raymond V. Mlecko, District Director, Chicago District, FDA, to John J. Halpin, President, Vandenberg Med-Tech Equipment, Inc. (March 24, 1999); Warning Letter from Patricia C. Ziobro, District Director, San Francisco District, FDA, to Russell Morgan, President, RC/Mor/All Med (Sept. 3, 1998); Warning Letter from Gary C. Dean, District Director, Denver District Office, FDA, to John Drewett, Corporate Risk Manager, Lincare, Inc. (Feb. 6, 1998).

[36] See Attachment 3 for a list of some of the more significant changes made to the Fresh Air requirements in 1998 and 1999.

IV. CGA/NWSA's Members Will Suffer Irreparable Injury if the Stay is not Granted

The failure of the FDA to grant the stay requested in this Petition will result in irreparable injury to the CGA/NWSA and their members. The continued presentation and publishing of Fresh Air speeches/documents, and the subsequent availability of previous Fresh Air documents, will subject CGA/NWSA's members to erratic, inconsistent, and unlawful requirements, and result in direct, substantial, and irreparable injury to CGA/NWSA's members. As a result of this arbitrary and, therefore, unlawful regulation, CGA/NWSA's members are potentially subject to unwarranted Warning Letters and other enforcement actions, possibly including plant shut downs, product seizures, and product recalls, all stemming from potential noncompliance with Fresh Air "requirements." In turn, these enforcement actions could result in excessive regulatory burden because CGA/NWSA's members must formally respond to such unwarranted actions, and develop and implement corrective actions with no opportunity for public debate on what in fact is "feasible and valuable" in contributing to assurance of drug safety, quality, and purity. [37] Moreover, the addition and removal of requirements at a rapid pace, with no opportunity to develop a meaningful understanding of these requirements, increases the industry's burden of and confusion with compliance. FDA's actions undermine the ability of CGA/NWSA's members to efficiently provide medical gas products to their customers, and, ultimately, could also endanger patients through unwarranted supply interruptions.

If the FDA denies this Petition for Stay, it is probable that CGA/NWSA's members will continue to be subject to unlawful requirements. The Agency has been promulgating Fresh Air standards since 1995 and, even after CGA/NWSA and individual companies brought the illegality of these activities to the Agency's attention, FDA has continued to regulate in this manner. Without relief from the improper imposition of regulatory requirements by means of Fresh Air, CGA/NWSA and their members will continue to be subject to the aforementioned inappropriate, excessive, and arbitrary regulatory burden, and will thereby be irreparably harmed.

V. CGA/NWSA's Case Is Not Frivolous and Is Being Pursued in Good Faith

Federal law, and the facts presented above, provide a sound basis for CGA/NWSA's challenge to FDA's unlawful regulation of cGMP requirements for medical gases. Consequently, CGA/NWSA's case is not frivolous. Moreover, CGA/NWSA's good faith in pursuing this matter is demonstrated by its previous efforts to bring the illegality of FDA's enforcement of Fresh Air standards to the Agency's attention, while continuing to attempt to comply with these constantly evolving requirements. Additionally, as another show of its good faith and consistent with its mission of developing safety standards and safe practices for its members, CGA has been working, since January 1999, to develop consensus standards for the medical gases industry through its Guideline 2000 ("G2K") project, and has sought the FDA's

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[37] FDA, Human Drug CGMP Notes (Volume 4, No. 1, Dec. 1996).

participation in this process. Indeed, CGA believes there is no better measure of its good faith than its repeated attempts to involve the FDA in its G2K project.[38]

VI. There Are Sound Public Policy Grounds Supporting the Stay

There are sound public policy grounds for the FDA to grant the stay that CGA/NWSA requests in this Petition. FDA's continued presentation and publishing of Fresh Air speeches/documents, and the continued availability of previous Fresh Air documents, violate federal law and create significant confusion and unpredictability in the medical gas industry. FDA's mission is to protect the public health, while facilitating the provision of safe and effective medical products and services to patients. The Agency's continued presentation and publishing of Fresh Air speeches/documents, and the continued availability of previous Fresh Air documents, unnecessarily increase compliance costs for industry, and therefore increase costs for consumers, while offering no verifiable improvement in the protection of patients. Moreover, the alternative to continued dissemination of Fresh Air programs and documents is proper promulgation of lawful guidance and regulations using notice and comment procedures.

VII. The Delay Resulting From the Stay Is Not Outweighed by Public Health or Other Public Interests

The granting of a stay will forward an important public interest by assuring that the proper application of statutes and regulations currently in effect are not contravened by FDA's continued unlawful regulation of cGMP requirements for medical gases, and will not result in delaying the Agency from taking necessary and proper regulatory actions. Agency regulation of the medical gas industry can only continue as long as it is done pursuant to proper administrative procedures. Delay of future presentations of Fresh Air, which FDA has now characterized as merely "outreach and training," could not possibly implicate the public health or other important public interests. Accordingly, the stay will serve, rather than contravene,

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[38] FDA met with CGA to discuss the G2K process on May 13, 1999, and indicated that the Agency would be involved in this initiative. Thus far, however, the FDA has chosen not to consult or interact actively or passively with CGA about the G2K process, and specifically, has not responded to requests made by CGA on October 25, 1999 and on January 4, 2000 for FDA to develop a process for Agency review and comment on the draft G2K documents. See letter from Joseph Famulare, Director, Division of Manufacturing and Product Quality, Office of Compliance, Center for Drug Evaluation and Research, FDA, to Carl T. Johnson, President of CGA, (January 21, 2000). In March of 2000, CGA submitted to the FDA for comment the first three G2K documents (CGA G13 - General Guide for Medical Gas Manufacturers; CGA M-1 - Guideline for Medical Gas Installations at Consumer Sites; and CGA P8.2 - Air Separation Unit and Trailer Filler Validation Guideline for Oxygen U.S.P. and Nitrogen N.F.). To date, CGA has heard nothing from the Agency.

important public interests by ensuring that lawful cGMP requirements for medical gases are developed and enforced.

VIII. Conclusion

The Famulare Memorandum alone is not sufficient to stop the damage from continued dissemination of Fresh Air. CGA/NWSA therefore maintain that the program itself must be ended, and cGMP requirements for medical gases be developed pursuant to a more formalized – and legally required – notice and comment procedure. Until that is accomplished, the continued dissemination of Fresh Air programs and materials will perpetuate the inappropriate and unlawful regulatory burden on the industry and regulatory confusion and uncertainty in the Agency, the industry and the public.

For the above-described reasons, CGA/NWSA respectfully request, pursuant to Section 701(h) of the FDCA, 21 U.S.C. § 371(h), the Agency's proposed regulations at 21 C.F.R. § 10.115, the Agency's regulations at 21 C.F.R. §§ 10.90(b)(9), 10.40(b), and Sections 4 and 10(e) of the APA, 5 U.S.C. §§ 553, 706, that the FDA promptly stay: (1) presenting, conducting, publishing, or otherwise promulgating Fresh Air speeches/documents that delineate cGMP requirements for compressed medical gases; and (2) the continued dissemination of previous Fresh Air speeches in any form.

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Attachments